REMARKS

1. Status of the Claims

Claims 1, 8, 9, 11-15, 21 and 26 are pending. Claims 1, 8, 9, 11, 12, 14, 15, 21, and 26 stand rejected. Claim 13 stands objected to for depending from a rejected claim; it is otherwise allowable. Claims 2-7, 10, 16-20, and 22-25 stand cancelled.

Applicants introduced new claims 27-30, which has support, for example, in the original as filed claims; on page 32, line 9 to page 34, line 2; Examples 6-7; and page 18, line 23.

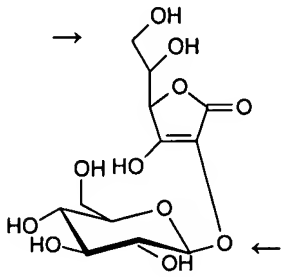
2. Status of the Rejections

Applicants note that the rejections stated in the Office Action mailed July 31, 2006 under 35 U.S.C. § 112, second paragraph and under 35 U.S.C. § 102(b) stand withdrawn. The finality of the prior Office Action was withdrawn, because the Office asserts new grounds of rejection.

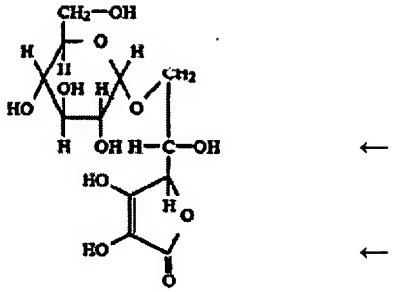
3. Rejections under 35 U.S.C. § 102

Claim 1 stands rejected under 35 U.S.C. § 102(b) allegedly as anticipated by Sakai et al. (U.S. Pat. No. 5,407,812) [hereinafter "Sakai"]. Sakai is cited for allegedly disclosing 2-O-β-D-glucopyranosyl-L-ascorbic acid as taught in claim 1. The Office cites to column 2, line 23 in support of its allegation that the reference anticipates claim 1.

Applicants traverse the rejection. In order for a reference to anticipate a claim, it must anticipate all limitations of the claim. The cited material from Sakai provides a structure that is not the same as that of claim 1 and is not 2-O-β-D-glucopyranosyl-L-ascorbic acid. The structure of claim 1 is presented on the left. The structure cited at col. 2, line 23 is provided on the right. The structures are distinguishable.



Claim 1



Sakai, col. 2, line 23

Sakai's formula II structure depicted at col. 2, line 23 is a 6-O-α form. Applicants' claimed compound is a 2-O-β form. These are clearly distinguishable and the 6-O-α form neither teaches nor suggests claim 1.

If the Office was referring to column 3, line 23, which recites "2-O-β-D-glucopyranosyl-L-ascorbic acid", this is clearly a typographical error on the part of Sakai given what the patent as a whole teaches. *See e.g.,* Abstract; col. 1, lines 9-11; col. 3, lines 27-41 and lines 63-66. Additionally, Applicants note that Sakai states:

> **Studies on the β-D-glucopyranosyl type derivatives of L-ascorbic acid confirmed that they hardly exhibit desired physiological activities in living body, especially, in humans.** Furthermore, conventional organic chemical processes have the drawbacks that they are inferior in economical efficiency because the reaction is very complicated and low in yield, and the establishment of non-toxicity and safeness for the resultant derivatives is very difficult.
>
> As described above, the proposals of saccharide derivatives of L-ascorbic acid in the prior art have proved unsatisfactory in view of stability, safeness, physiological activity and economical efficiency, and not been practiced hitherto.
>
> The present invention has as an object to overcome the drawbacks of conventional saccharide derivatives of L-ascorbic acid. More particularly, we studied a novel saccharide derivative of L-ascorbic acid which is obtainable by a biochemical process utilizing a saccharide-transfer reaction.
>
> As disclosed in the specification of Japanese Patent Application No. 127,072/89, we discovered a novel substance, an α-glycosyl-L-ascorbic acid, especially, 2-O-α-D-glucopyranosyl-L-ascorbic acid, which is free from direct reducing activity, superiorly stable, readily hydrolyzable in vivo, and satisfactorily high in physiological activity, as well as developing its preparation

> and uses in foods, beverages, pharmaceuticals for susceptive diseases, and cosmetics.

See col. 2, lines 46-65. Sakai is clearly directed 2-O-α-D-glucopyranosyl-L-ascorbic acid, i.e. an alpha form. Thus, Sakai is directed to the alpha form and specifically teaches away from any beta form of L-ascorbic acid. Accordingly, Sakai does not teach or suggest claim 1. As the Office has failed to present a *prima facie* case of anticipation, the rejection should be withdrawn, and claim 1 allowed.

4. Rejections Under 35 U.S.C. § 103

Claims 1, 8, 9, 11-12, 14-15, 21 and 26 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Sakai et al. as applied above, in view of Kawada et al. (U.S. Pat. No. 4,754,026) ["Kawada"]. The Office asserts that Sakai allegedly teaches the non-acetylated compound of 2-O-β-D-glucopyranosyl-L-ascorbic acid. Sakai is also asserted for allegedly teaching "to make their compounds using a saccharide-transferring enzyme...." Office Action, ¶3, page 4. It is also cited for teaching "an amount of 0.001% or more is acceptable for use of their alpha-derivative...." *Id.* Sakai also purportedly teaches "that their composition may be used in various forms, such as cosmetic, pharmaceutical, or dietary uses...." *Id.* The Office admits that Sakai does not teach acetylated derivatives recited by claims 8 and 9, nor does Sakai teach methods of using the β-derivatives.

The Office relies on U.S. Patent No. 4,754,026 issued to Kawada et al. for teaching "that saccharides are protected with acetyl groups at the 2', 3', 4' and 6' positions." Office Action, page 4. Allegedly, it would have been obvious at the time to protect the saccharide with the acetyl groups, because purportedly the use of acetyl groups as protecting agents in saccharide chemistry is very well known. The Office goes on to assert that Sakai teaches methods of making their compounds using L-ascorbic acid and the α-glucosyl saccharide and saccharide transferring enzyme. Based on these assertions, the Office concludes it would have been obvious to make the β-derivatives as instantly claimed with the methods of making the α-glucosyl derivatives. The Office admits that Sakai is drawn to the use of the alpha-derivative. Yet, the Office asserts that a composition is allowable only if no utility is asserted for the old compound.

Applicants traverse. As stated above, Sakai does not teach 2-O-β-D-glucopyranosyl-L-ascorbic acid (claim 1). Sakai further does not teach or suggest 2-O-(tetra-O-acyl-β-D-

glucopyranosyl) ascorbic acid (claim 8). Sakai is directed to alpha forms of L-ascorbic acid *only*.

The defects of Sakai are not cured by Kawada. Kawada teaches the conversion of uracil derivatives to cytosine derivatives. The relied upon section of Kawada only states: "The hydroxyl groups in these glycosyl groups are protected with protecting groups usually used for protection of the hydroxyl groups in the sugar, such as acyl (e.g., acetyl, benzoyl) and benzyl." Kawada, col. 2, lines 62-66. This section fails to provide any suggestion or teaching which would have motivated a skilled person to convert the α-form of Sakai to the β-form now claimed. In fact, given the portion of Sakai recited above, there is nothing in Kawada that overcomes the teaching away from β-forms as put forth by Sakai. Thus, Kawada fails to cure the defects of Sakai.

Applicants observed numerous unexpected and numerous beneficial properties including for example the protecting effect against cell death of human skin epidermal keratinocytes induced by UVB irradiation (Example 8), the effect on intracellular ascorbic acid concentration in human skin epidermal keratinocytes (Example 9), promoting collagen synthesis by normal human dermal fibroblasts (Example 10), intestinal absorption in the rat (Example 11), and the impact of cell population doubling on human dermal fibroblasts (Example 12). The observed effects for the β form are all greater than the α-form of Sakai, as set forth in all but Example 11 of Applicants' specification. Applicants further provide the article of Norio Muto et al., "*Formation of a Stable Ascorbic Acid 2-Glucoside by Specific Transglucosylation with Rice Seed α-Glucosidase*," AGRIC. BIOL. CHEM., 54(7): 1697-1703 (1990). The Muto reference illustrates further failure in obtaining 2-O-β-D-glucopyranosyl-L-ascorbic acid.

Accordingly, the Office has not adduced a *prima facie* case of obviousness as to claims 1 and 8. Additionally, these references cannot teach compositions comprising these compounds, i.e. the provitamin, pharmaceutical, and cosmetic compositions of claims 14-15, 21 and 26.

The Office cites to *Ex parte Erdmann*, 194 U.S.P.Q. 96 (Bd. Pat. App. & Int. 1975) and *Ex parte Douros*, 163 U.S.P.Q. 667 (Bd. Pat. App. & Int. 1968) for its position. However, given the facts discussed above, neither *Erdmann* or *Douros* apply to the current facts. Applicants note that Sakai teaches away from using the β-form as discussed. There would be no motivation to combine the references, because in Sakai's mind, the protecting

groups taught by the secondary reference would fail to curb the defects of the β-forms, and which is why Sakai et al. pursued the alpha forms. Kawada fails to address the teaching away, and does not serve to overcome Sakai's defects. Additionally, Sakai does not teach the claimed compounds (claims 1 and 8), methods of making these compounds, or any of the compositions comprising the compounds. Accordingly, there is no *prima facie* case of obviousness adduced for claims 1, 8, 9, 11-12, 14-15, 21, and 26. Therefore, Applicants respectfully request withdrawal of the rejection, and allowance of the claims.

CONCLUSION

In view of the above arguments and amendments to the claims, Applicants respectfully assert that the claims are condition for allowance and respectfully request a Notice of Allowance.

Should any issues remain outstanding or if there are any questions concerning this paper, or the application in general, the Examiner is invited to telephone the undersigned representative at the Examiner's earliest convenience. Should any outstanding fees be owed or overpayments credited, the Commissioner is invited to charge or credit Deposit Account No. 50-0573 accordingly.

Respectfully submitted,

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